Medication Assisted Treatment

Claudie H. Jimenez MD MS

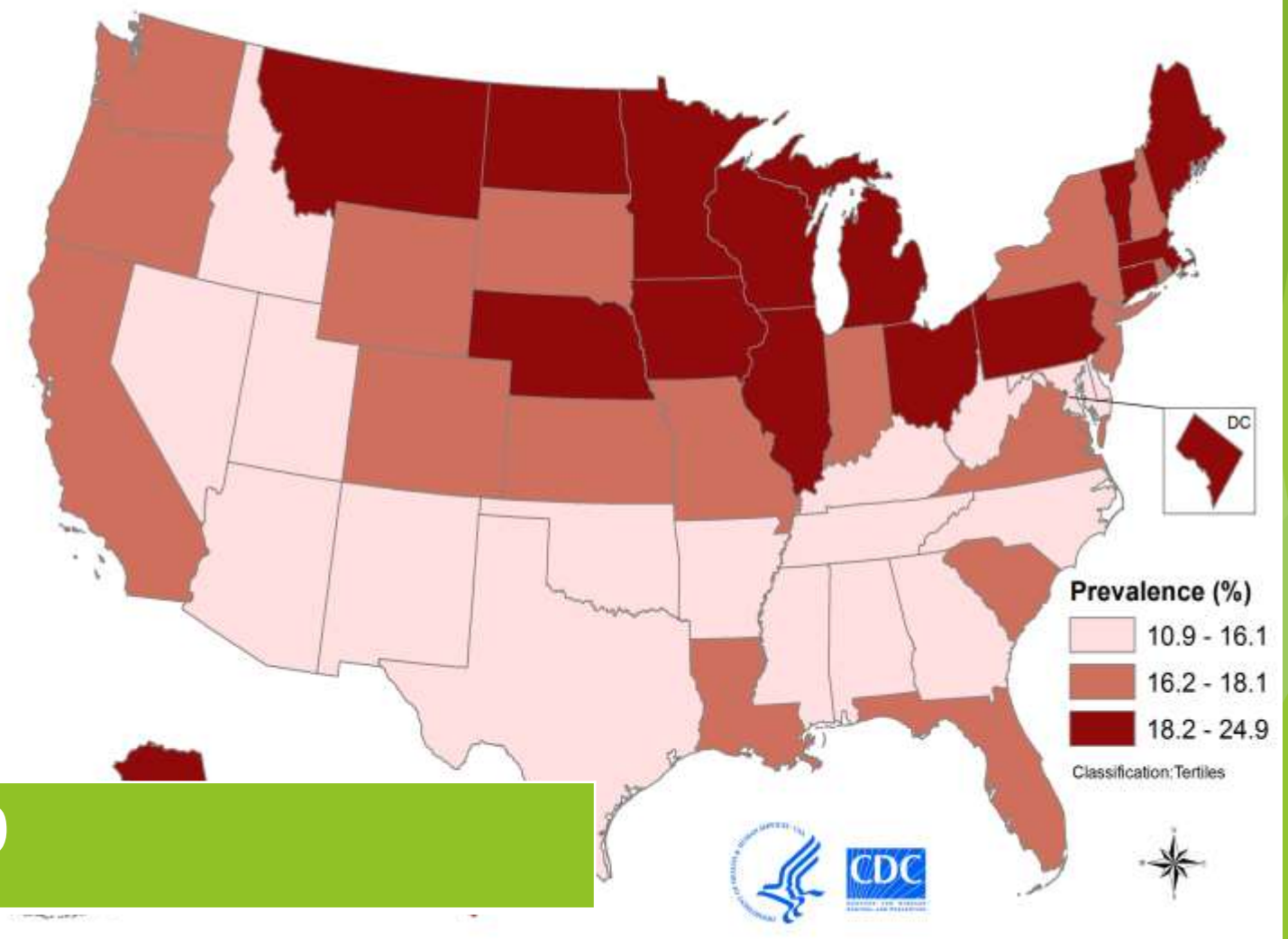
Objectives

Define	Define Medication Assisted Treatment
Describe	Describe Medications Used for Treatment
Understand	Understand how Medication Assisted Treatment fits into a patient's recovery from Addiction

Background

Alcohol Use

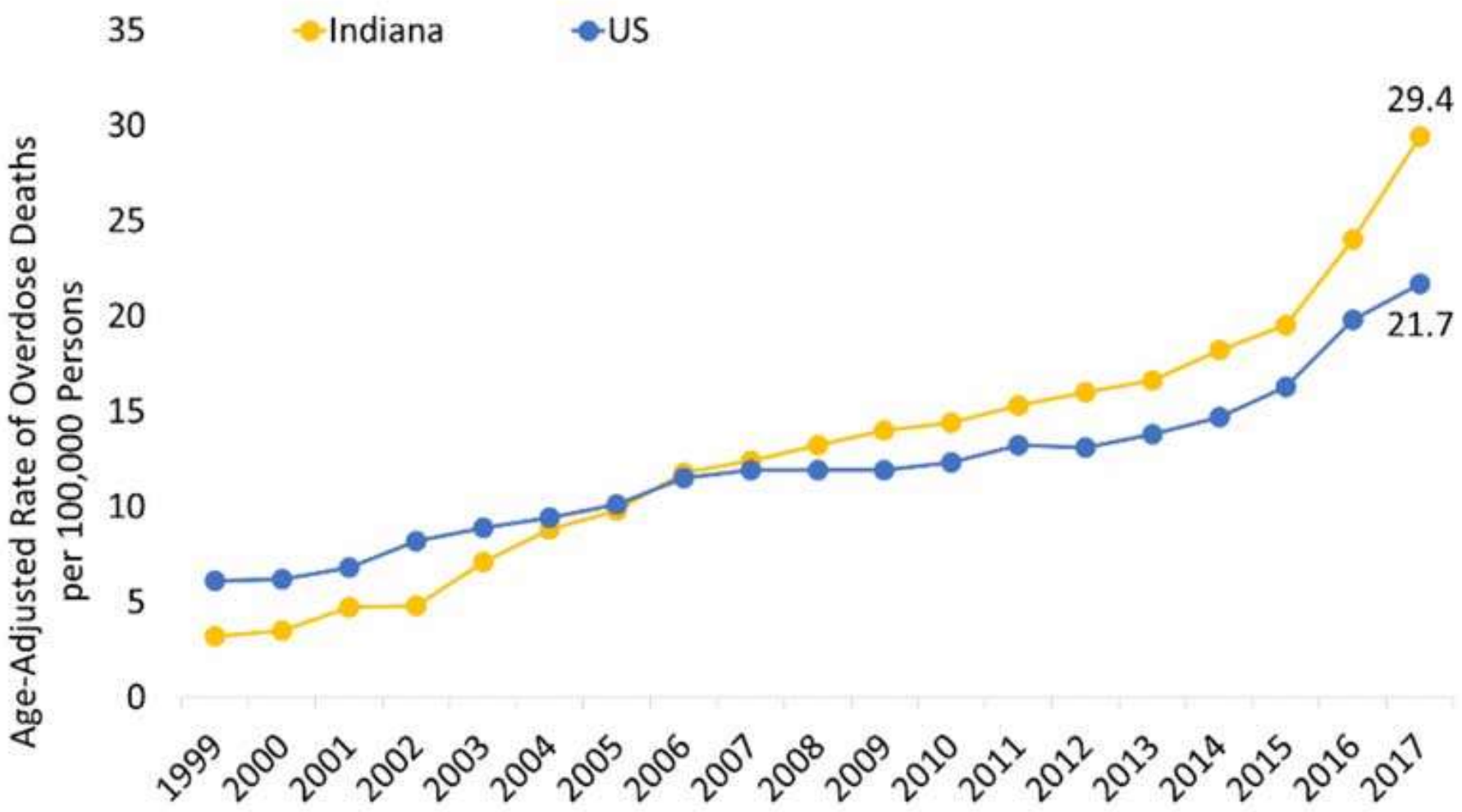
- 6% of Adult population reports heavy drinking use
- 17% of Adult population reports binge drinking



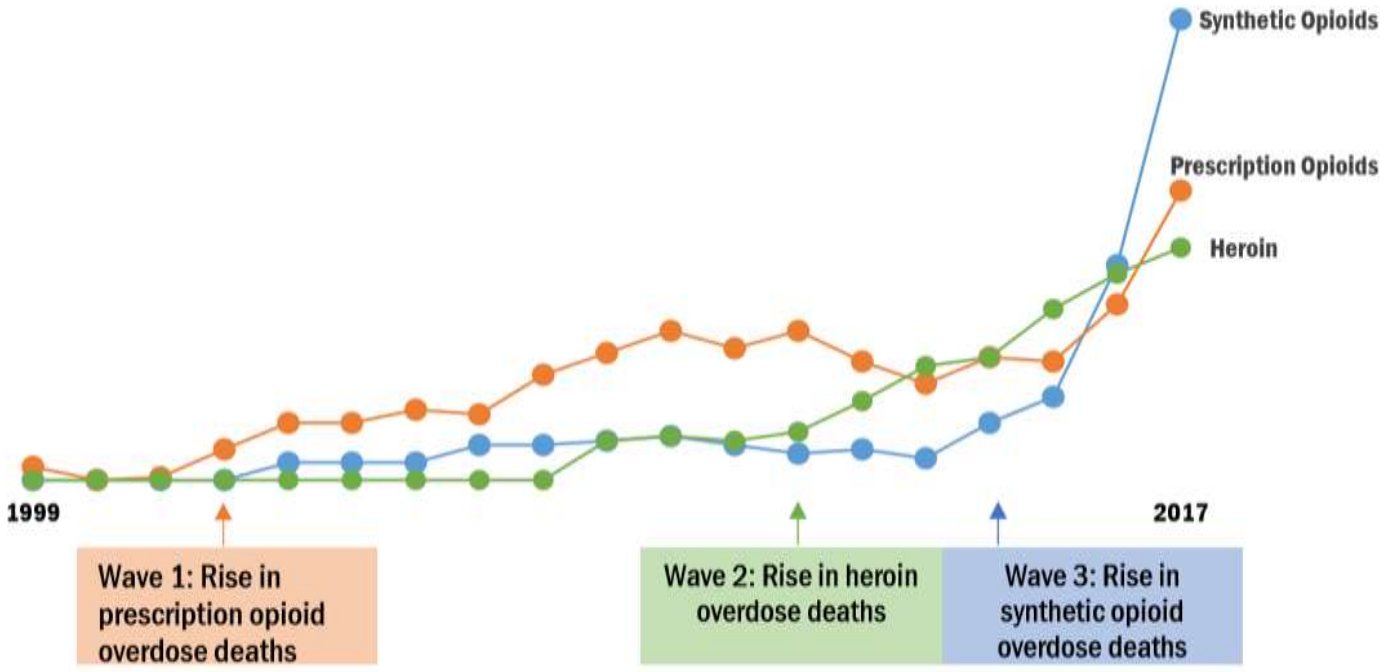
COST Indiana	$4,468,200,000

Division of Population Health , National Center for Chronic Disease Prevention and Health Promotion , Centers for Disease Control and Prevention

Background

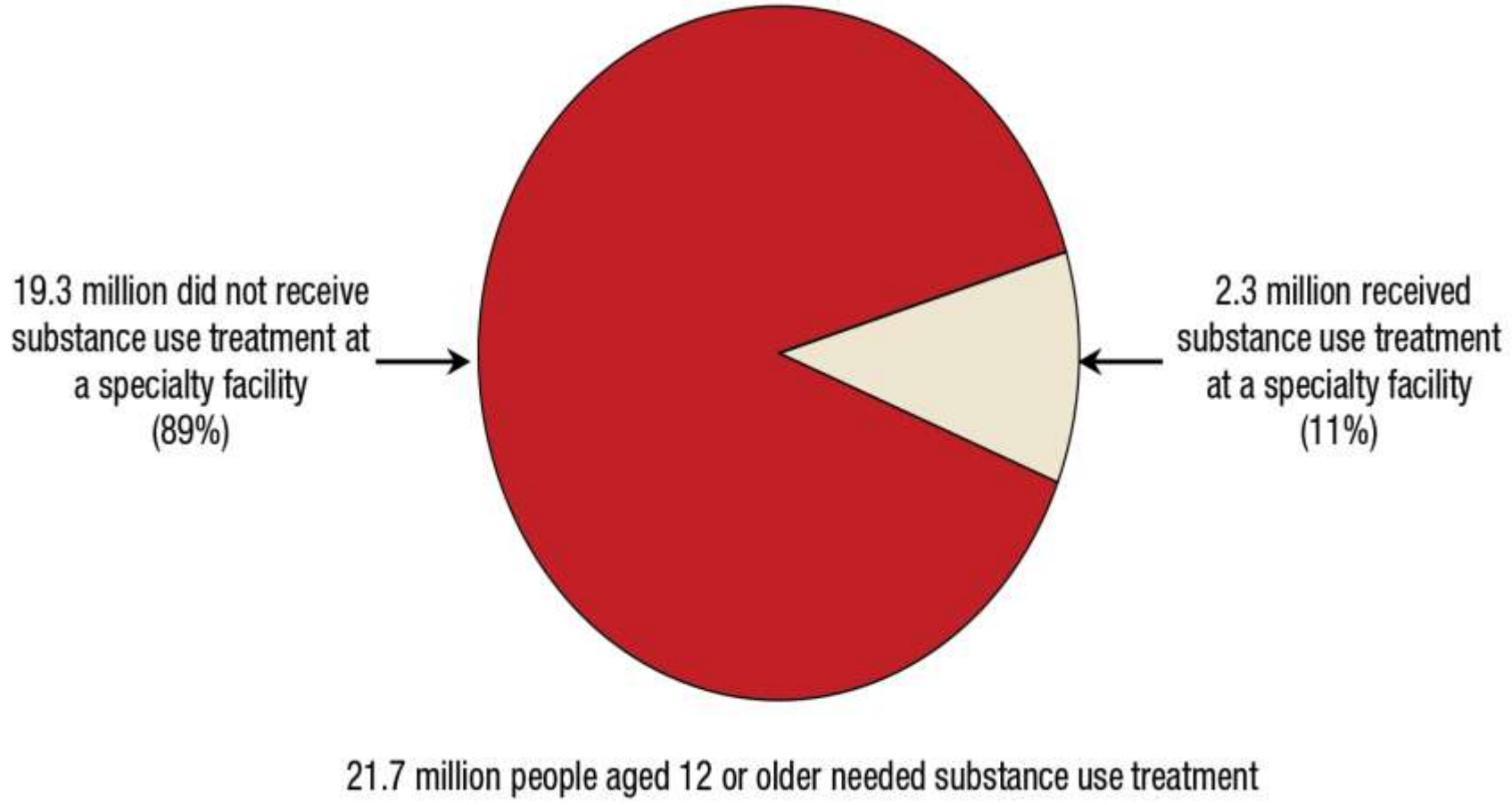

Indiana
US
Age-Adjusted Rate of Overdose Deaths per 100,000 Persons
35
30
25
20
15
10
5
0
29.4
21.7
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017

Indiana Opioid Overdose Deaths 1999-2017



The Drug Overdose Epidemic in Indiana: Behind the Numbers Data Brief, Published April 3rd, 2019https://www.in.gov/isdh/27393.htm

Background: Patients with SUD (including alcohol)That Received Treatment 2015



Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health (NSDUH), 2015.

Definition of Addiction

- From the American Society of Addiction Medicine:

"Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. "

Chronic Disease

- Addiction: A Chronic Brain Disease

"Chronic"
Requires a wholistic approach to helping people manage their illness

"Brain"
People must fight stigma and moral blaming

"Disease"
Medical approach can be effectively used for treatment

Science Matters

FRONTIERS IN NEUROSCIENCE: THE SCIENCE OF SUBSTANCE ABUSE

Addiction Is a Brain Disease, and It Matters

Alan I. Leshner

Scientific advances over the past 20 years have shown that drug addiction is a chronic, relapsing disease that results from the prolonged effects of drugs on the brain. As with many other brain diseases, addiction has embedded behavioral and social-context aspects that are important parts of the disorder itself. Therefore, the most effective treatment approaches will include biological, behavioral, and social-context components. Recognizing addiction as a chronic, relapsing brain disorder characterized by compulsive drug seeking and use can impact society's overall health and social policy strategies and help diminish the health and social costs associated with drug abuse and addiction.

Dramatic advances over the past two decades in both the neurosciences and the behavioral sciences have revolutionized our understanding of drug abuse and addiction. Scientists have identified neural circuits that subsume the actions of every known drug of abuse, and they have specified common pathways that are affected by almost all such drugs. Researchers have also identified and cloned the major receptors for virtually every abusable drug, as well as the natural ligands for most of those receptors.

drug user or, worse, an addict. The most beneficent public view of drug addicts is as victims of their societal situation. However, the more common view is that drug addicts are weak or bad people, unwilling to lead moral lives and to control their behavior and gratifications. To the contrary, addiction is actually a chronic, relapsing illness, characterized by compulsive drug seeking and use (*1*). The gulf in implications between the "bad person" view and the "chronic illness sufferer" view is tremen-

affects both the health of the individual and the health of the public. The use of drugs has well-known and severe negative consequences for health, both mental and physical. But drug abuse and addiction also have tremendous implications for the health of the public, because drug use, directly or indirectly, is now a major vector for the transmission of many serious infectious diseases—particularly acquired immunodeficiency syndrome (AIDS), hepatitis, and tuberculosis—as well as violence. Because addiction is such a complex and pervasive health issue, we must include in our overall strategies a committed public health approach, including extensive education and prevention efforts, treatment, and research.

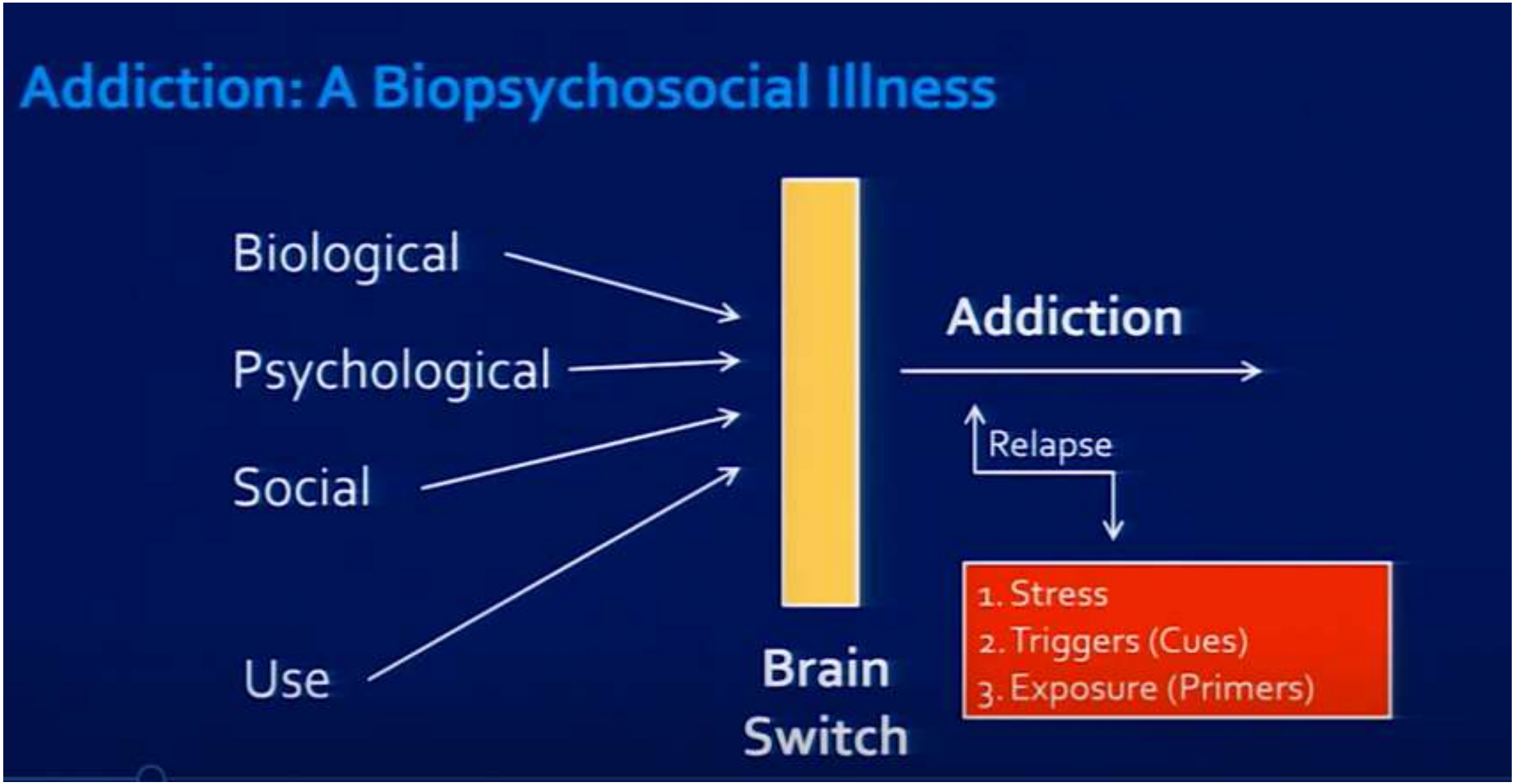
Science is providing the basis for such public health approaches. For example, two large sets of multisite studies (*3*) have demonstrated the effectiveness of well-delineated outreach strategies in modifying the behaviors of addicted individuals that put them at risk for acquiring the human im-

DSM V Criteria Substance Use Disorder

1. Taking _____ in larger amounts and for longer than intended
2. Wanting to cut down or quit but not being able to do it
3. Spending a lot of time obtaining the _____.
4. Craving or a strong desire to use
5. Repeatedly unable to carry out major obligations at work, school, or home due to use
6. Continued use despite persistent or recurring social or interpersonal problems caused or made worse by opioid use
7. Stopping or reducing important social, occupational, or recreational activities due to opioid use
8. Recurrent use in physically hazardous situations
9. Consistent use despite acknowledgment of persistent or recurrent physical or psychological difficulties from using
10. Develop tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount. (Does not apply for diminished effect when used appropriately under medical supervision)
11. Develop withdrawal symptoms manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (Does not apply when used appropriately under medical supervision)

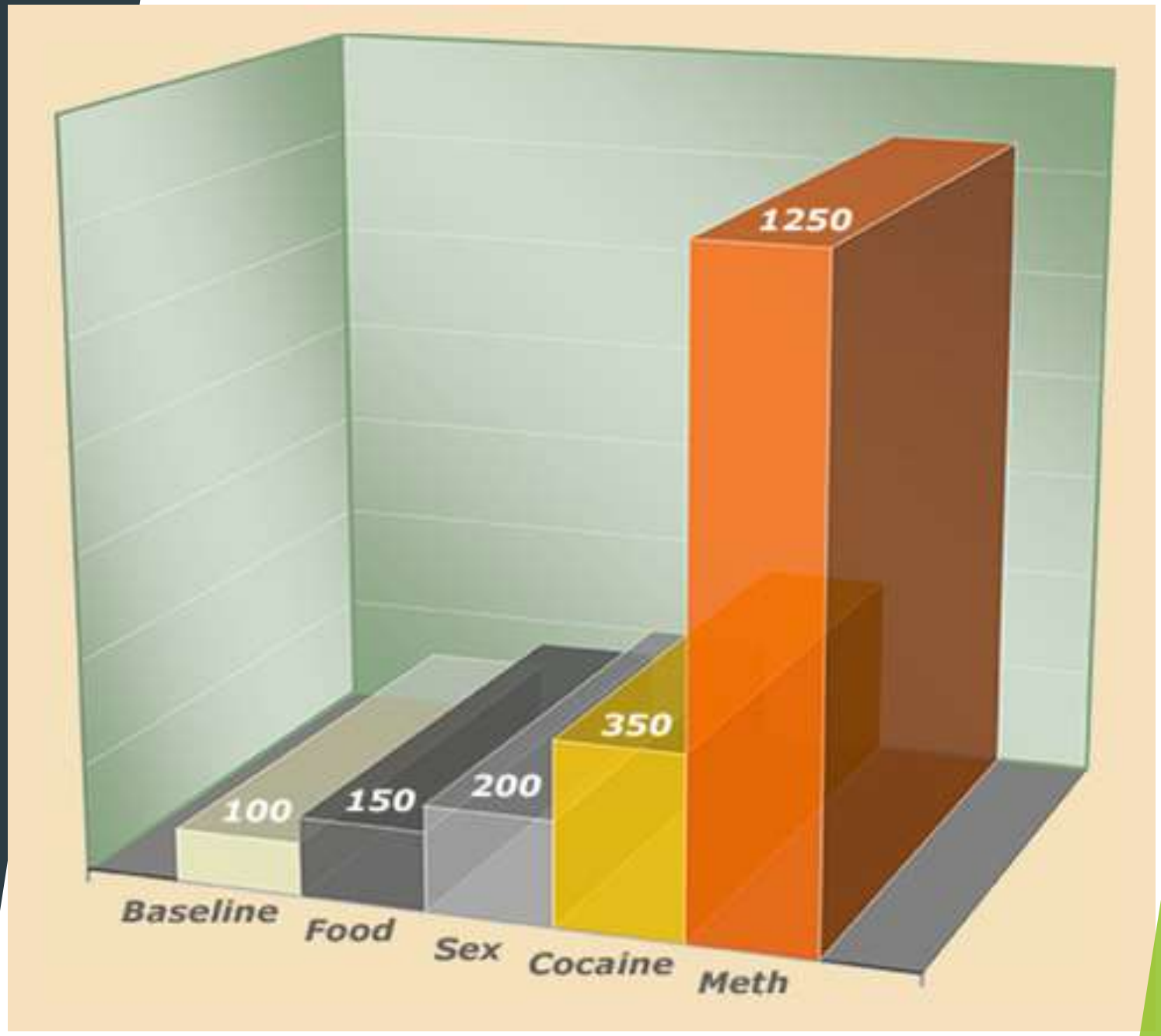
Risk Factors

- Genetics
- Exposure
- Stress

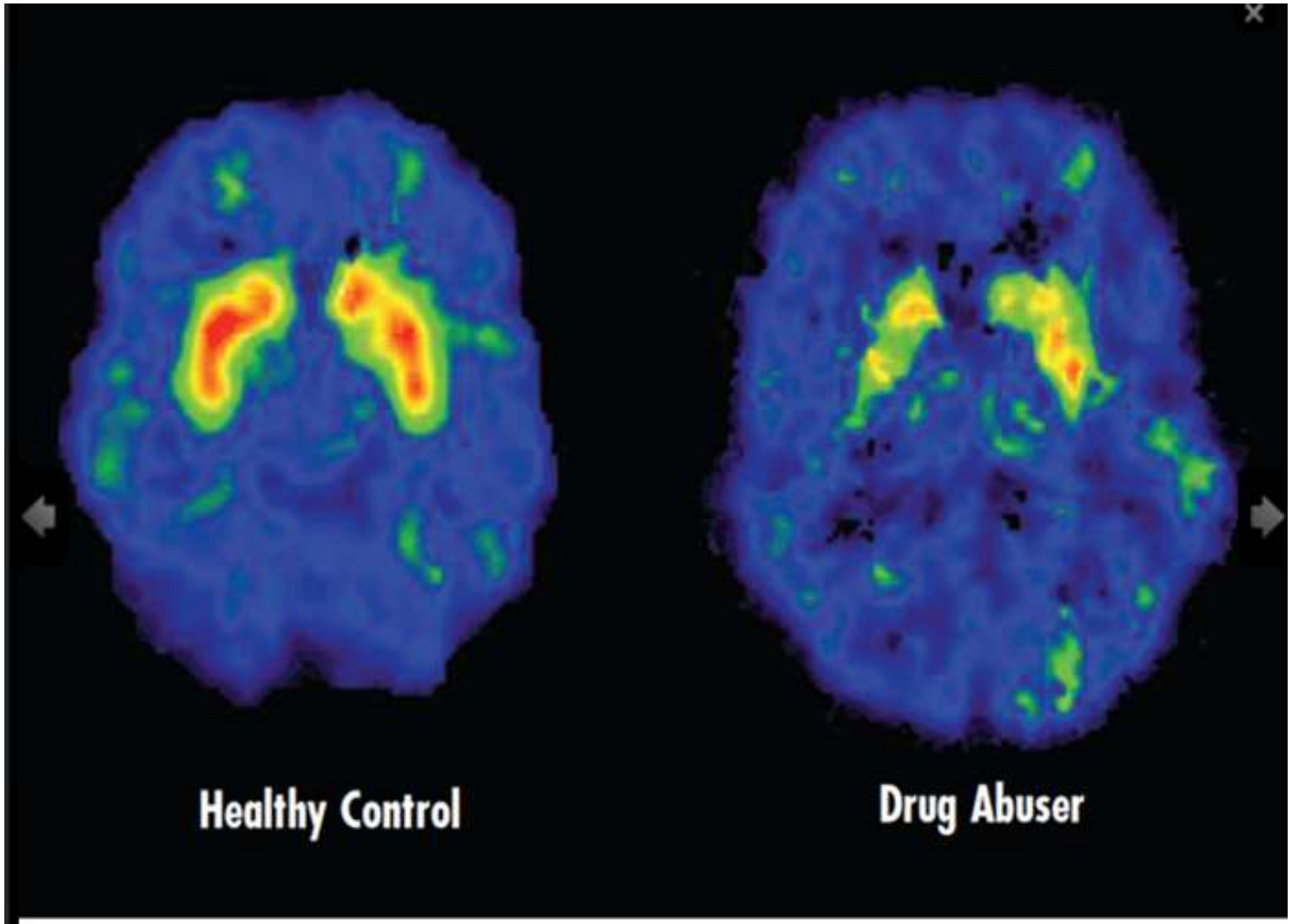

Addiction: A Biopsychosocial Illness
Biological
Psychological
Social
Use
Brain Switch
Addiction
Relapse
1. Stress
2. Triggers (Cues)
3. Exposure (Primers)

Biological Pleasure Response

- Its' all about Dopamine



Addiction changes the Brain



Decreased Dopamine Transporters in a Methamphetamine Abuser[18]

Medication Assisted Treatment

- Any treatment that includes a medication as part of that treatment
- Substance Use disorders with FDA approved Medication for Treatment:
  - Alcohol Use Disorder
  - Opioid Use Disorder
  - Nicotine Use Disorder

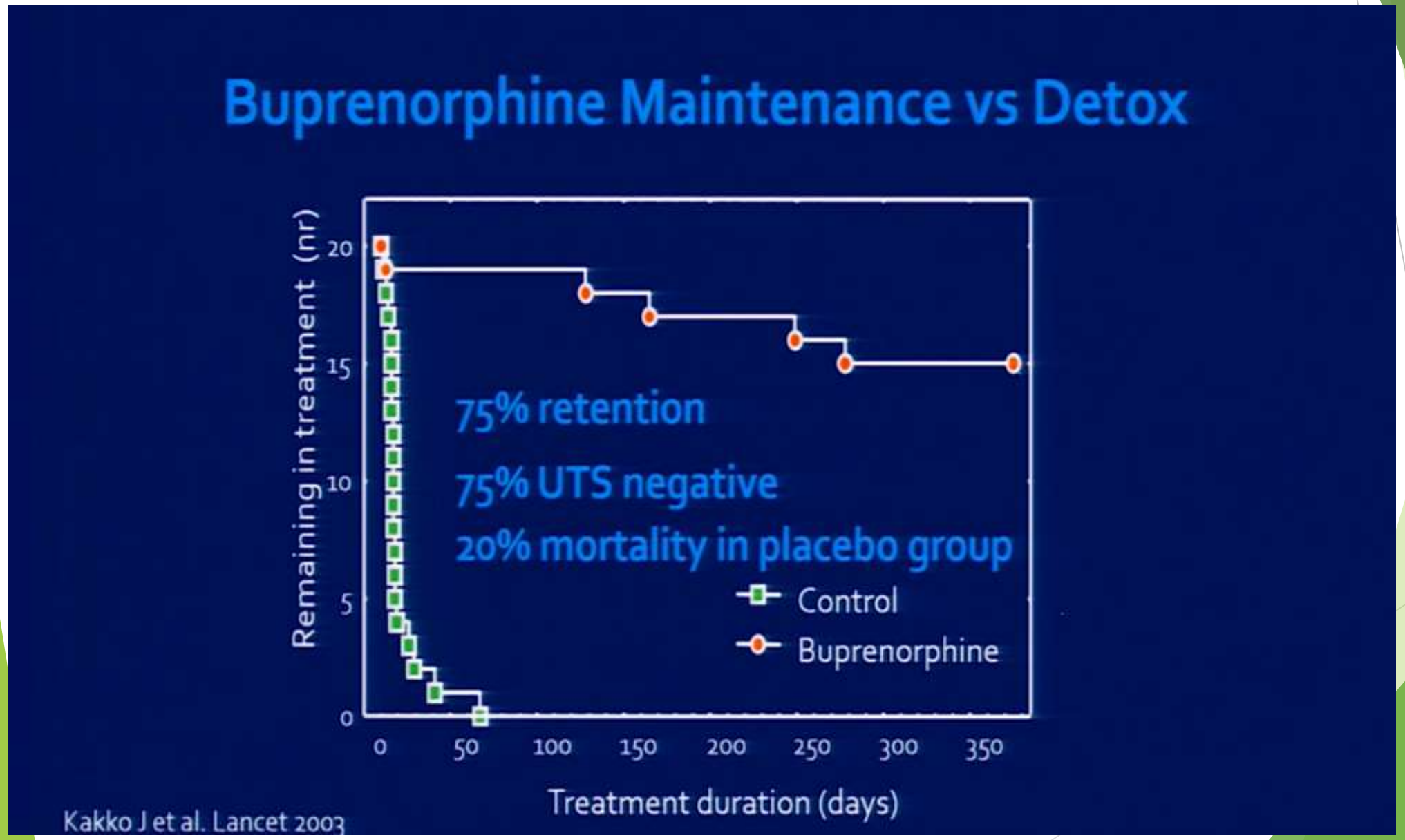
Basis for Medication Use

- Drugs of Abuse work on very specific receptors in the brain and nervous system
- Medications used in the treatment of substance use disorder are used to their effects on these specific receptors in the brain and nervous system
- Medications have very specific efficacy based on their molecular structure

Basis for Medication Use Continued

- Medications have been used for decades in the detoxification process
- FDA has approved several medications to help manage the disease of addiction
- MAT is listed as part of CDC recommended strategies to reduce overdose deaths
- Medications are a prescribed part of a comprehensive treatment plan
- Medications are used to treat virtually every other medical condition including hypertension and diabetes
- Science has identified that several changes take place in the brain's chemical structure that are not corrected quickly
- MAT allows the patient to think more clearly without the physiologic distractions taking away from treatment.
- Most reliable predicator of successful recovery and positive outcomes is length of time in treatment
  - MAT keeps patients in treatment longer

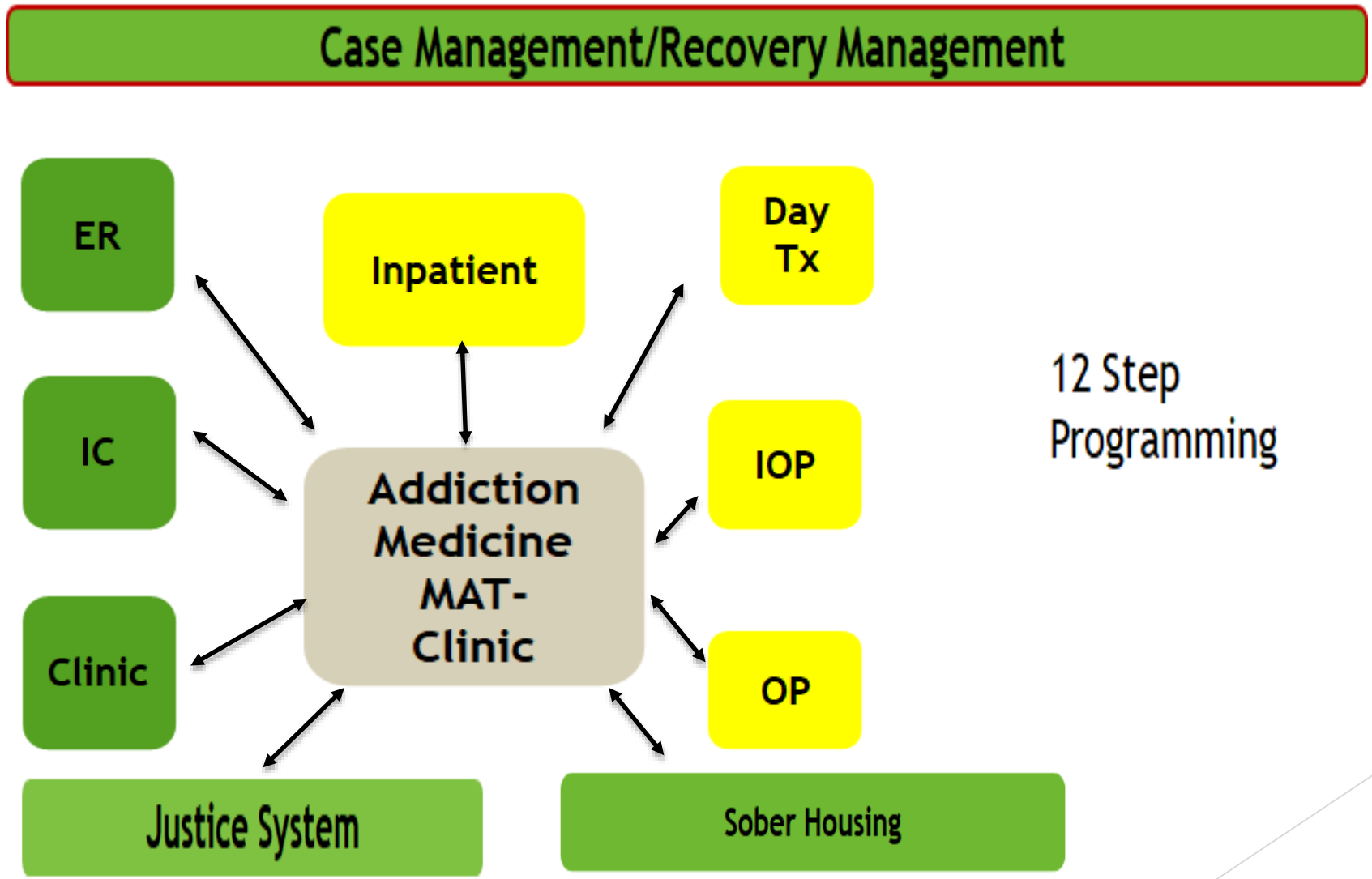
Retention in Treatment MAT vs. Detox



Chronic Disease Adherence to Treatment

- Type 1 Diabetes: 60%
- Hypertension: Less that 40%
- Asthma: Less than 40%
- Substance Use Disorder: 40-60%

Fully Integrated Recovery Home



12 Step Programming

Alcohol Use Disorder Medications for Treatment

- Naltrexone (Revia/Vivitrol)
  - Approved for use in Alcohol Use Disorder in 1994
  - Decreases craving for alcohol and relapse to heavy drinking
  - Decreases euphoric effects from alcohol and reinforcing properties
  - Two Forms: Oral and Extended Release Injection (Vivitrol)
    - Better compliance with Injection
- Acamprosate (Campral)
  - Approved for use in Alcohol Use Disorder in 2004
  - Decreases relapse rate
  - Associated with less quantity and frequency of drinking
  - Patients must take 3 pills, 3 times a day which is a challenge for compliance

Alcohol Use Disorder Medications for Treatment (Continued)

- Disulfiram (Antabuse)
  - Approved for use in Alcohol Use disorder in 1949
  - Alcohol Sensitizing agent
    - Make drinking alcohol drinking unpleasurable or even toxic
  - Very poor compliance to medication
  - Lack of evidence showing its effectiveness in relapse prevention

- Other Medications
  - Antidepressants
  - Anti-anxiety (NOT BENZODIAZEPINES)

Effectiveness of MAT for Alcohol

- Study #1
  - Meta-analysis of naltrexone and acamprosate 2013
  - Review of 64 Randomized Controlled Studies from 1970-2009
  - Both medications were found to be effective in treating Alcohol Use Disorder
    - Naltrexone had more of an effect on heavy drinking and cravings
    - Acamprosate had a larger size effect on abstinence alcohol
    - Acamprosate became less effective if patient relapsed on to alcohol
    - Both medications were more effective in maintaining abstinence if patient was detoxed prior to starting medication.

Maisel NC, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful?. *Addiction*. 2013;108(2):275–293.

Effectiveness of MAT for Alcohol

- STUDY #2
  - Inpatients admitted for alcohol related disorders
  - >100 Patients in study
  - Discharge program starting Naltrexone prior to discharge showed significant decrease in hospital readmission and ED visits.
  - Large Urban Hospital in San Fransisco
  - Results:
    - Return to ED within 30 Days: 8.2% (received MAT) vs. 23.4% (did not receive MAT)
    - Readmission or ED presentation within 30 days: 12.0% (Received MAT) vs 38.5 % (did not received MAT)
      - Most presentations in both groups were alcohol related

Wei et al: Treatment and Discharge Planning Protocol for Alcohol Dependence
J Gen Intern Med 30(3):365–70

Effectiveness of MAT for Alcohol Criminal Justice System

- Surprisingly not much in medical literature
- STUDY #2
- Incarcerated population with co-occurring Severe Mental Illness
- Retrospective Study looking at over 5000 patients total
- Used multiple medications including Campral (most utilized), Naltrexone and Disulfiram

- Results:
  - MAT group: Increased treatment utilization and decreased ED visits compared to Non MAT group
  - No statistical difference in recidivism

Am J Psychiatry. 2018 Jul 1; 175(7): 665–673.

Opioid Use Disorder Medications

- Methadone
  - Full opioid Agonist
  - Risk for overdose
  - Long acting: Dose once daily
  - No wait time to start treatment
  - Interactions with other medications
  - Can have cardiac side effects
  - Highly regulated and high barrier to treatment (patients must go to clinic for daily dosing)

Opioid Use Disorder Medications

- Naltrexone
  - Opioid antagonist
  - Patients must be opioid free 5-7 days prior to starting medication
  - No risk of overdosing from medication directly
  - Decreases cravings for opioids
  - Can elevate Liver Function Tests
  - Not a controlled substance
  - Can be given in an office setting
  - Comes in depo injectable form (Vivitrol)

Opioid Use Disorder Medications

- Buprenorphine
  - Partial opioid agonist
  - Oral, injectable* and implant available**
  - Lower risk of overdose (respiratory depression ceiling)
  - Controlled Substance
  - Can be given in an office setting
  - Prescriber must have X DEA waiver
  - Less medication interactions
  - Can elevate Liver Function Tests

*FDA approved no studies available showing long term effectiveness

**FDA approved not well integrated into care; multiple practical challenges

Table 2

Pharmacological Profile of Methadone, Buprenorphine, and Naltrexone

	Methadone	Buprenorphine	Naltrexone
Main effect	Mu full agonist, NMDA antagonist	Mu partial agonist	Mu antagonist
Bioavailability	70%–80%	50%	< 50% (~100% ER)
Half-life	28 hours	37 hours	9 hours (4.95 days ER)
Clinically apparent drug interactions	Rifampin, phenytoin, several ART	Select ART	Opioids NSAIDS (?)
Active metabolites	None	Nor-buprenorphine	6-beta-naltrexol

ART Antiretroviral therapy; NSAID Non-steroidal anti-inflammatory; ER extended release formulation

J Addict Dis. 2012 Jul; 31(3): 207–225.
doi: 10.1080/10550887.2012.694598

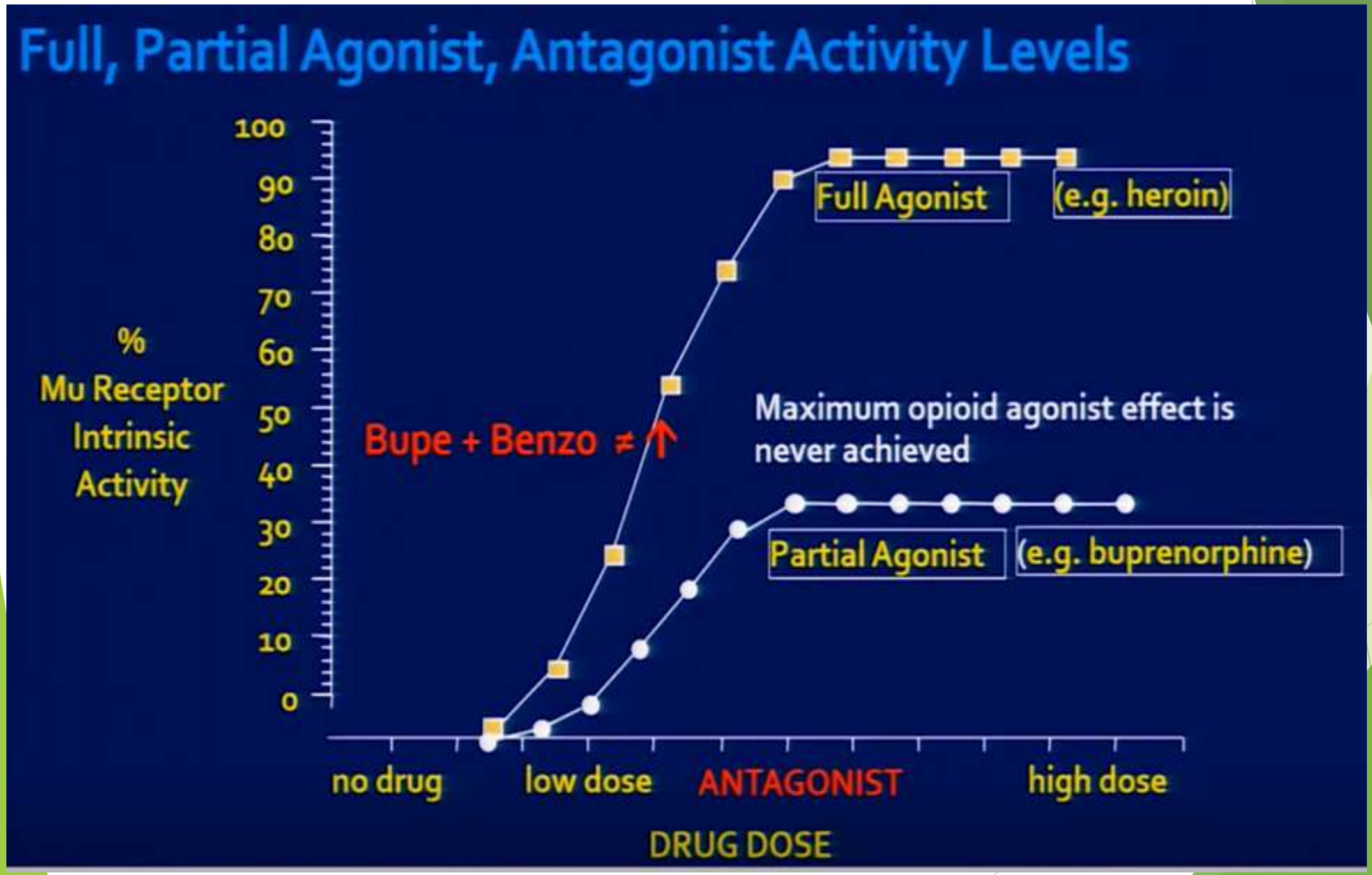

Full, Partial Agonist, Antagonist Activity Levels
% Mu Receptor Intrinsic Activity
100
90
80
70
60
50
40
30
20
10
0
Full Agonist
(e.g. heroin)
Bupe + Benzo ≠ ↑
Maximum opioid agonist effect is never achieved
Partial Agonist
(e.g. buprenorphine)
no drug
low dose
ANTAGONIST
high dose
DRUG DOSE

Table 1

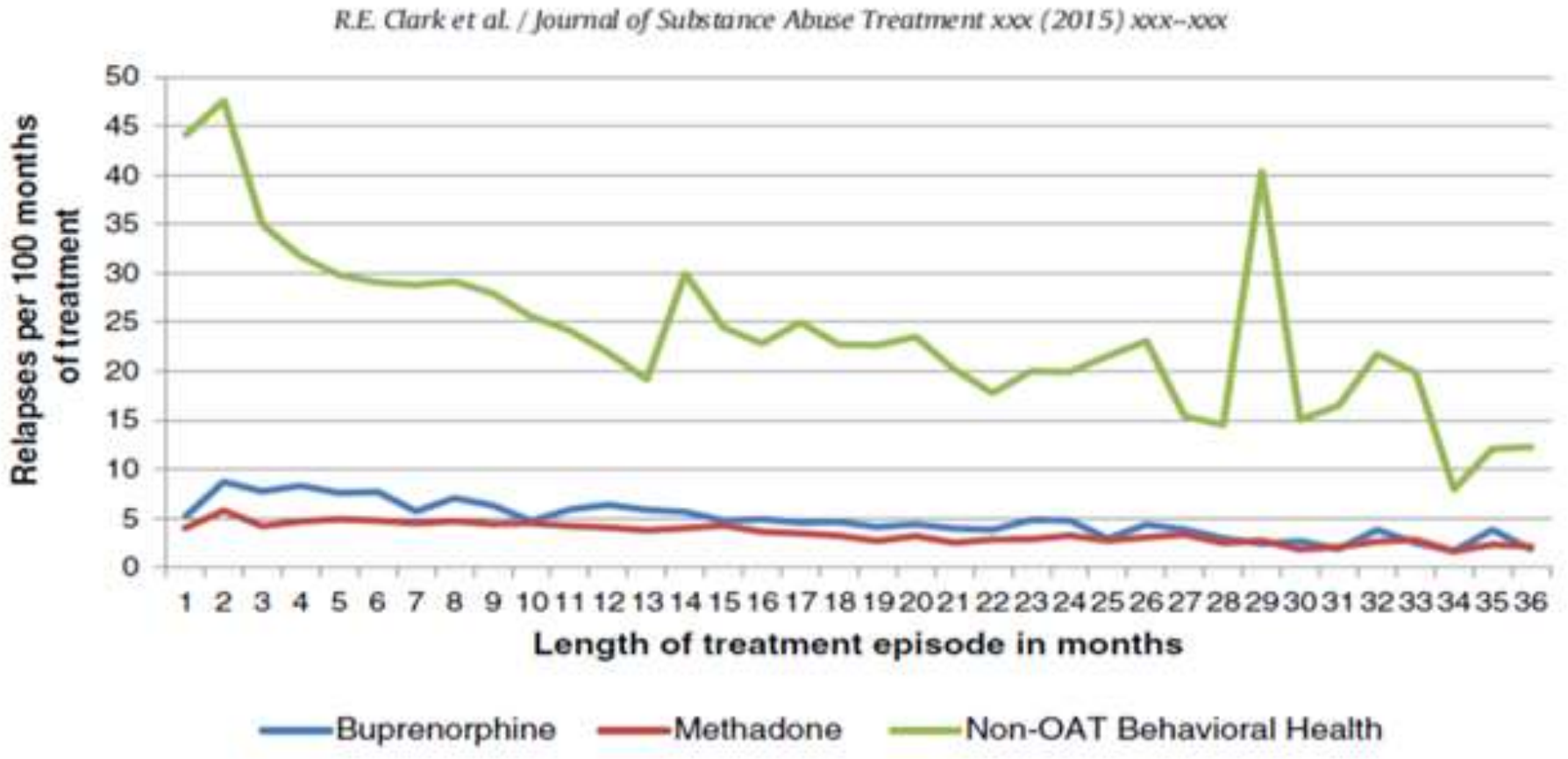
Clinical Characteristics of methadone, buprenorphine, and naltrexone

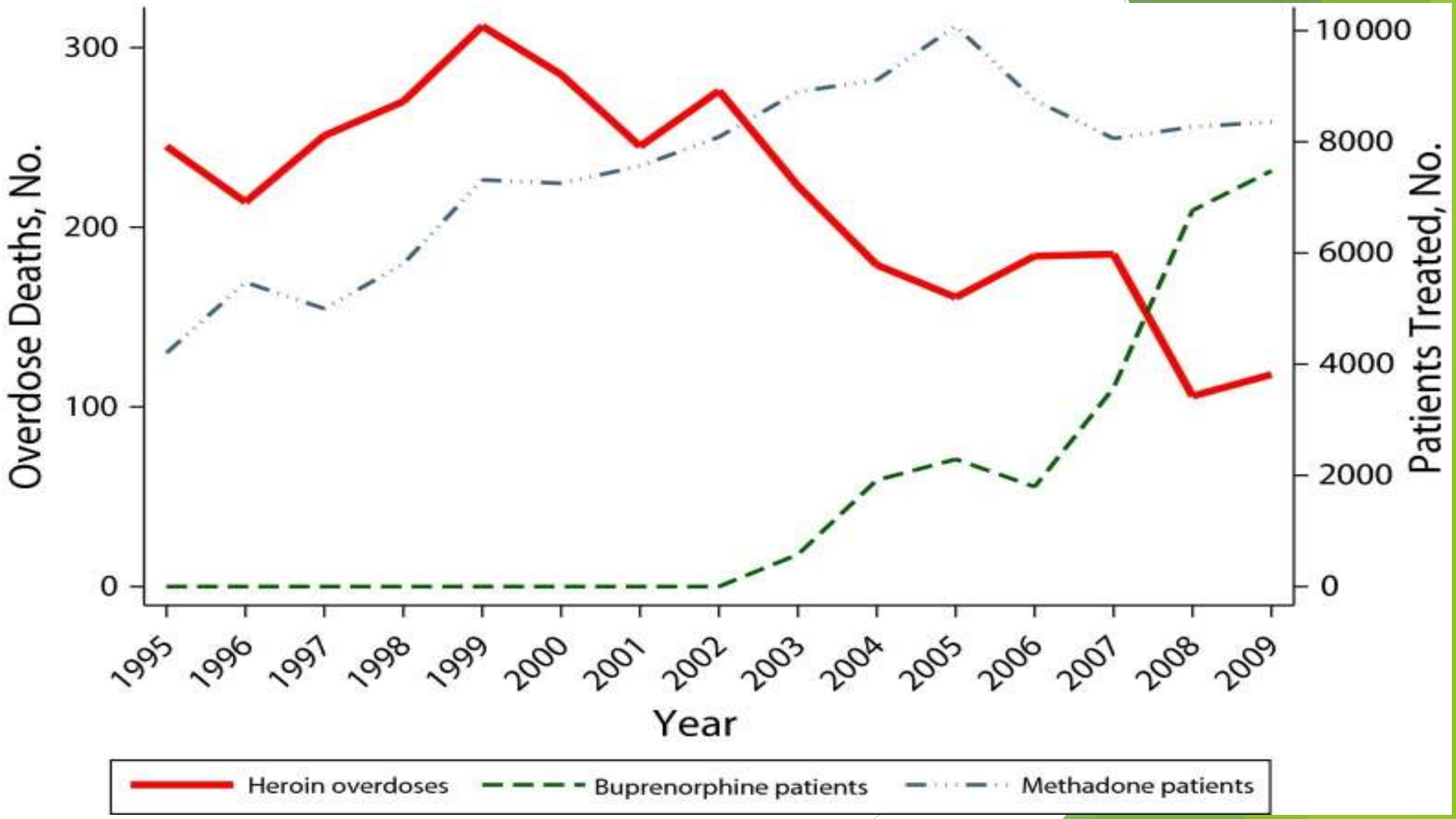
	Methadone	Buprenorphine	Naltrexone
Controlled substance	Yes	Yes	No
Availability	OTP	OTP or DATA Waived practitioner	Any prescribing practitioner
1-year retention	60%	60%	20% (53% 6-months ER)
Direct expense	$	$$	$$–$$$$
Dosing frequency	Daily	Daily	Daily or monthly (ER)
Narcotic blockade	Yes, at steady-state	Yes, at steady-state	Yes
Can induce withdrawal	No	Yes	Yes
Overdose potential	Yes	Yes	No
Withdrawal upon cessation	Yes	Yes	No
Loss of tolerance on cessation	Yes	Yes	Yes
Complicates treatment of moderate-severe pain	No	No	Yes

OTP opiate treatment program; DATA Drug Addiction Treatment Act of 2000; ER extended release formulation

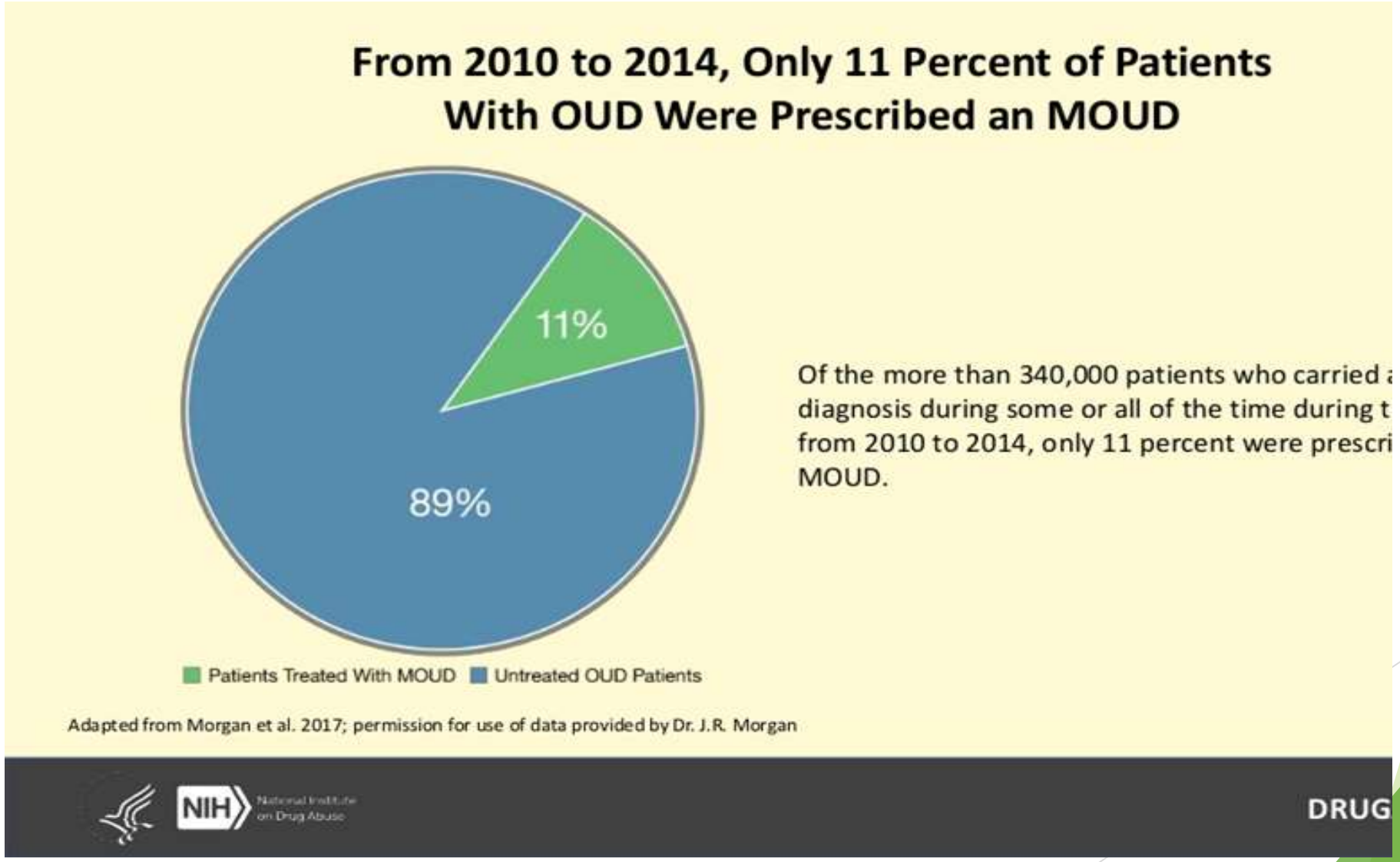
J Addict Dis. 2012 Jul; 31(3): 207–225.
doi: 10.1080/10550887.2012.694598

Relapse Rate of Patients on MAT




Overdose Deaths, No.
300
200
100
0
Patients Treated, No.
10 000
8000
6000
4000
2000
0
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
Year
Heroin overdoses
Buprenorphine patients
Methadone patients

Background: Patients with OUD that Receive MAT



Incarcerated Population

- 24% of prison population meet criteria for Alcohol Use Disorder
- 30% of prison population meet criteria for other Drug Use Disorder
  - Women prisoners up to 50%

- Only 11% of prisoners who meet criteria for any substance use disorder receive any treatment

Addiction. 2017 Oct;112(10):1725-1739. doi: 10.1111/add.13877. Epub 2017 Jun 28
https://www.prisonerhealth.org/educational-resources/factsheets-2/incarceration-substance-abuse-and-addiction/

MAT Use Pre and Post Release Incarceration

- Study #1
- Western MA County Jail
- Forty-seven Patients
- XR-NTX approximately 7 days prior to release,
  - 2 groups Pre and Post Release
  - Rate of retention at week 4 was higher in group with treatment initiation prior to release week 4: 55% versus 25%; week 8: 36% versus 25%; week 24: 21% versus 15%
  - Three patients died from overdose at 3-5months after release and 2.5 or more months after stopping XR-NTX,

J Subst Abuse Treat. 2018 Feb;85:97-100. doi: 10.1016/j.jsat.2017.04.002. Epub 2017 Apr 6

MAT Use Pre and Post Release Incarceration

- Study #2
- Baltimore Jail
- 211 Patients
- Bup/Nal Started upon admission to Jail
  - 2 groups (Bup + Counseling) (Counseling only then referral for bup after release)
  - Present to treatment 47.5% of bup participants entered community treatment, while for the counseling only 33.7% participants entered community treatment. Three patients died from overdose at 3-5months after release and 2.5 or more months after stopping XR-NTX,

MAT and Incarcerated Populations

- Study #2
- Meta analysis 2019
- Compared Methadone, Buprenorphine and Naltrexone Treatment during and after incarceration delivered in prisons and jails
- Looked at Randomized controlled trial and quasi-experimental studies published through December 2017 that examined induction to or maintenance on methadone (18 studies), buprenorphine (3 studies), or naltrexone (3 studies) in correctional settings
- There were a sufficient number of methadone RCTs
- Too few buprenorphine or naltrexone studies
- Methadone provided during incarceration increased community treatment engagement, reduced illicit opioid use and injection drug use, but did not reduce recidivism
- Individual review of buprenorphine and naltrexone studies showed these medications were either superior to methadone or to placebo,or were as effective as methadone in reducing illicit opioid use post-release.
- More study is needed

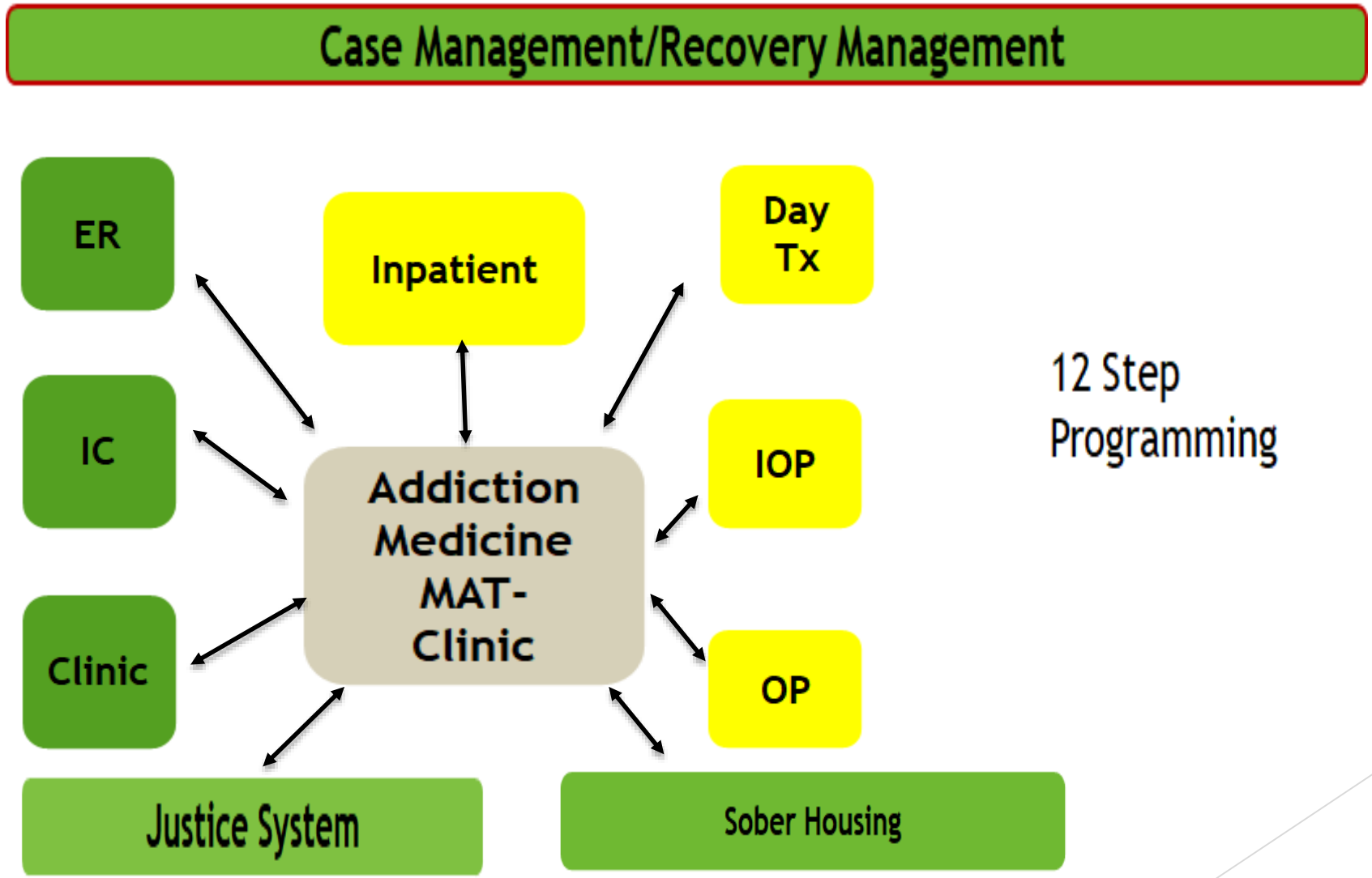
MAT for Smoking

- Nicotine Patches
  - Nicotine Replacement
  - Multiple Forms: patches, inhaler, gum
- Bupropion
  - Agonist α4β2 sub-type of the nicotinic receptor
  - Anti-depressant
  - Decreases Cravings for cigarettes
- Chantix
  - partial agonist selective for α β nicotinic acetylcholine receptor
  - Decreases cravings and pleasurable effects from smoking
  - Can have significant side effects

Other Substances

- Stimulants: Methamphetamine and Cocaine
  - Many studies on multiple different medications- nothing has been shown to be effective
  - There are no FDA approved medications
  - Behavioral Treatment is the recommended treatment
    - Contingency Management
    - Cognitive Behavioral Therapy
- Benzodiazepines
  - There is no MAT
  - Detox-not effective long term
  - Long taper
  - Cognitive Behavioral Therapy to Manage Anxiety and Insomnia
  - SSRIs can help manage anxiety

MAT as part of a Fully Integrated Recovery Home



12 Step Programming

MAT as part of Comprehensive Support for Communities, Patients and Families

- Incorporate MAT into a comprehensive treatment program for patients and families
- Increase access to Residential Treatment Programs
  - Utilize MAT in Residential Programs
  - Increase the number of beds
  - Provide Reimbursement for Services
- Increase Access to Peer Support
  - Appropriate Reimbursement for Peer Support Services
- Focus on Prevention
  - Education for Providers
    - Formal Addiction Training in Medical School, NP/PA School and Residency Programs
    - Training on Controlled Substance Prescribing-not just opioids
  - Community Education
    - Awareness of using controlled substances including prescriptions
    - Develop Resilience

Thank you!